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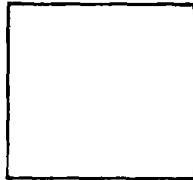
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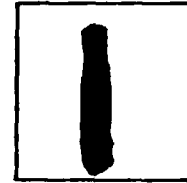
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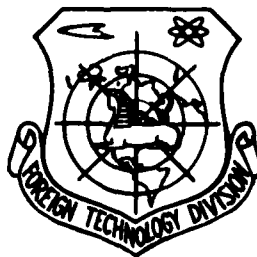
FOREIGN TECHNOLOGY DIVISION



AETHAPERAZINUM

by

G. N. Pershina



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UNEDITED MACHINE TRANSLATION

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Block	Italic	Transliteration	Block	Italic	Transliteration
А а	А а	A, a	Р р	Р р	R, r
Б б	Б б	B, b	С с	С с	S, s
В в	В в	V, v	Т т	Т т	T, t
Г г	Г г	G, g	У у	У у	U, u
Д д	Д д	D, d	Ф ф	Ф ф	F, f
Е е	Е е	Ye, ye; E, e*	Х х	Х х	Kh, kh
Ж ж	Ж ж	Zh, zh	Ц ц	Ц ц	Ts, ts
З з	З з	Z, z	Ч ч	Ч ч	Ch, ch
И и	И и	I, i	Ш ш	Ш ш	Sh, sh
Й й	Й й	Y, y	Щ щ	Щ щ	Shch, shch
К к	К к	K, k	Ъ ъ	Ъ ъ	"
Л л	Л л	L, l	Ы ы	Ы ы	Y, y
М м	М м	M, m	Ь ь	Ь ь	'
Н н	Н н	N, n	Э э	Э э	E, e
О о	О о	O, o	Ю ю	Ю ю	Yu, yu
П п	П п	P, p	Я я	Я я	Ya, ya

*ye initially, after vowels, and after Ъ, Ь; e elsewhere.
When written as ё in Russian, transliterate as yë or ë.

RUSSIAN AND ENGLISH TRIGONOMETRIC FUNCTIONS

Russian	English	Russian	English	Russian	English
sin	sin	sh	sinh	arc sh	sinh ⁻¹
cos	cos	ch	cosh	arc ch	cosh ⁻¹
tg	tan	th	tanh	arc th	tanh ⁻¹
ctg	cot	cth	coth	arc cth	coth ⁻¹
sec	sec	sch	sech	arc sch	sech ⁻¹
cosec	csc	csch	csch	arc csch	csch ⁻¹

Russian	English
rot	curl
lg	log

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AETHAPERAZINUM.

Aethaperazinum - new neuroplegic substance, in some relations (as anti-emetic, ataractic, and somniferous) stronger than aminazine, and is at the same time less toxic, than the latter.

Readings to the use/application of a preparation the same as for aminazine.

Aethaperazinum exerts the effect/action also on those patients who are not sensitive to the effect/action of aminazine.

PHARMAGOLOGICAL STUDY.

Aethaperazinum - dihydrochloride of 2-chloro- $\{\gamma[4-(\beta\text{-hydroxyethyl})\text{-piperazinyl-1}]\text{-propyl}\}$ -phenothiazine - a neuroplegic substance, synthesized in the section of the organic synthesis (head - candidate of chemical sciences S. V. Zhuravlev, junior scientific workers Ye. Z. Yermakov and A. M. Gritzenko) of the

institute of pharmacology and chemotherapy of AMN of the USSR. On the chemical structure aethaperazinum corresponds to the foreign preparations Chlorpiprozine, Decentan, Fentazin, Perphenazin, Trilafon.

Aethaperazinum is the white or cream with slightly pinkish hue fine-crystalline powder, readily soluble in water and physiological solution. With standing in light/world the solutions of aethaperazinum are decomposed/expanded and appears their pinkish staining. The solutions of aethaperazinum are incompatible with the solutions of barbiturates and carbonates; upon sterilization by boiling they do not lose activity.

The pharmacological study of aethaperazinum, carried out in the laboratory of particular pharmacology (candidate of medical sciences Yu. I. Vikhlyayev), showed that the new neuroplegic substance has the wide spectrum of activity, similar to the spectrum of the effect/action of aminazine.

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All means of the central effect/action in aethaperazinum are considerably stronger than in aminazine. The toxicity of aethaperazinum does not exceed the toxicity of the aminazine; some

means of the peripheral effect/action in aethaperazinum are expressed to a lesser degree.

Anti-emetic effect/action.

In experiment/experiences on dogs it was noted, that the intravenous introduction of aethaperazinum to the dose of 0.032 mg/kg for 30 minutes before the intravenous introduction of apomorphine to the dose of 0.021 mg/kg prevented vomiting in all experimental animals. The comparison of the anti-emetic activity of aethaperazinum and aminazine was conducted under identical conditions and it was based on determination of ED_{50} from the method of Litchfield and Wilcoxon. In this case it was established/installed, that ED_{50} aethaperazinum was equal to 0.0086 mg/kg (0.0056-0.0136), aminazine 0.082 mg/kg (0.046-0.148). The given in parentheses numerals indicate the confidence limits of ED_{50} with $P=0.05$.

Thus, aethaperazinum on the anti-emetic effect/action is 9.6 times more active than aminazine, and the relative activity of preparation, calculated taking into account equimolar relations, 18.98 times exceeds the activity of aminazine.

Effect on the conditioned-reflex activity of animals.

In experiment/experiences on rats employing a motor-defensive procedure it was established/installed, that aethaperazinum introduced subcutaneously at the dose of 0.4 mg/kg, suppresses the manufactured conditioned reflexes and inhibits the formation of temporary/time bonds. Aminazine caused the analogous effect/action only during the introduction of the doses, 8 times exceeding the doses of aethaperazinum.

In experiment/experiences on rats employing defensive procedure with the utilization of an extremely strong electric irritant (procedure, proposed by Knoll for evaluating the ataractic substances) aethaperazinum 4 times exceeded the activity of aminazine. With recount in equimolar relations the activity of aethaperazinum employing this procedure 7-8 times exceeds the same of aminazine.

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Sedative effect/action.

In all forms of the introduction of aethaperazinum - intravenous, oral, subcutaneous, intraperitoneal - to different forms/species of experimental animals (mouse, rat, rabbits, dogs, lowest monkeys) was observed the expressed sedative effect/action of

preparation. Animals became low-mobility and somnolent. Most effective was intravenous introduction.

The comparative activity of the sedative effect/action of aethaperazinum and aminazine was studied according to the method of Komlos, Knoll, Tardos and Sass. About the intensity of motor activity they judged by amount of liquid, displaced by animals (white rats) from register system, which served as time unit.

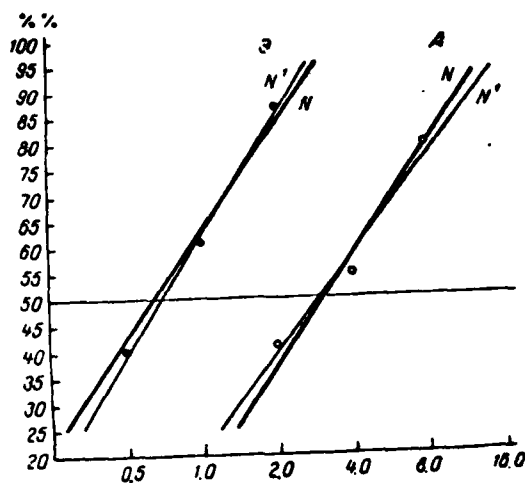


Fig. 1. Comparative evaluation of the sedative effect/action of aethaperazinum (E) and aminazine (A). Suppression of the spontaneous motor activity of rats. On the axis of ordinates - percentage of the suppression of motor activity with respect to the initial level; on the axis of abscissas - dose in the logarithmic scale; N - obtained values; N' - corrected values.

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In this case it was established/installed, that aethaperazinum at the dose of 0.75 mg/kg half decreases the motor activity of animals, while the aminazine exerted the analogous effect/action only during the introduction of the dose of 4 mg/kg.

The calculation of relative activity showed that aethaperazinum is 4.73 times more active than aminazine (Fig. 1). In recount to equimolar relations the relative activity of aethaperazinum is equal to 9.36.

Central-weakening the effect/action of aethaperazinum is expressed in the fact that it, similar to aminazine, causes the weakening of the musculature of animals due to effect on the toning functions of brain.

Combined effect/action with narcotic and somniferous substances.

During the study of the comparative activity of aethaperazinum and aminazine according to the capacity to strengthen and to prolong the effect/action of somniferous, narcotic and analgesic substances in experiment/experiences on mice (involution of hexenal, Nembutal and hydrochloride) it is established/installed, that both substances possess approximately identical activity (table).

Effect on blood circulation and respiration.

In experiment on the animals, that are located under narcosis and decerebrated, is noted the expressed hypotensive and adrenolytic effect/action of aethaperazinum. During introduction to the doses of

0.1-0.5 mg/kg it decreases the pressor vascular reactions, caused by the overcompression of carotid arteries, by the stimulation of sensitive nerve trunks and by the introduction of adrenalin; to large doses - 3-5 mg/kg - a preparation completely removes the vascular reactions, caused by the introduction of adrenalin and by the overcompression of carotid arteries. In this case sometimes is observed the distortion of reaction to adrenalin. Aethaperazinum, just as aminazine, is decreased and completely is removed the contracture of the third epoch of cat, caused by the introduction of adrenalin and by the stimulation of the postganglionic cut of neck sympathetic nerve. In comparison with aminazine the hypotensive and adrenolytic effect/action of aethaperazinum is expressed to a lesser degree. The intravenous introduction of aethaperazinum does not cause noticeable changes in the respiration of animals.

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In experiment/experiences on the isolated/insulated organs/controls and on the animals, that are located under narcosis and decerebrated, aethaperazinum exerts the weak cholinolytic, antihistaminic and spasmolytic effect/action.

Aethaperazinum in concentration $2 \cdot 10^{-6}$ decreases, and in concentration $5 \cdot 10^{-5}$ it completely prevents the contracture of intestine, caused by acetylcholine ($6 \cdot 10^{-7}$). In concentration $2 \cdot 10^{-7}$ the preparation decreases, while in concentration $2 \cdot 10^{-6}$ prevents the spasm of the intestine of guinea pig, caused by histamine ($8 \cdot 10^{-7}$).

The comparative activity of aethaperazinum and aminazine.

(1) Вид действия	(2) ED в мг/кг		(5) Относительная активность	(6) Относительная активность в эквимолекулярных отношениях
	(3) аэтаперазин	(4) аминазин		
(7) Противорвотное	0,0086 (0,0056—0,0136)	0,0821 (0,046—0,148)	9,6 (4,5—20,4)	18,98 (8,8—40,3)
(8) Гнетение оборонительных условных рефлексов	0,245 (0,182—0,328)	1,95 (1,57—2,42)	7,96 (5,5—11,5)	15,74 (10,8—22,7)
(9) Седативное			4,74 ± 0,52	9,36 ± 1,03
(9a) Атарактическое	0,55 (0,51—0,6)	2,2 (1,53—3,14)	4,0 (2,75—5,8)	7,8 (5,39—12,5)
(10) Продление действия наркотических веществ:				
(11) гексенала			0,74	1,45
(12) нембутала			0,77	1,5
(13) хлоралгидрата			0,6	1,19
(14) Токсическое (LD ₅₀):				
(15) мыши	960 (865—1070)	520 (485—560)	0,54 (0,47—0,69)	1,0 (0,9—1,3)
(16) крысы	405 (367—453)	155 (117—204)	0,38 (0,28—0,51)	0,72 (0,53—0,96)

Key: (1). Means of the effect/action. (2). ED in mg/kg. (3). aethaperazinum. (4). aminazine. (5). Relative activity. (6). Relative activity in equimolecular relations. (7). Anti-emetic. (8). Suppression of defensive conditioned reflexes. (9). Sedative. (9a). Ataractic. (10). Prolongation of effect/action of narcotic substances. (11). hexenal. (12). Nembutal. (13). chloralhydrate. (14). Toxic. (15). mouse. (16). rat.

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The study of the comparative activity of aethaperazinum and aminazine the cholinolytic, antihistaminic and spasmolytic effect/action showed that both preparations barely differ from each other in the appropriate means of activity.

Acute/sharp and chronic toxicity.

The determination of the acute/sharp toxicity of aethaperazinum was carried out in experiment/experiences on mice and rats with the subcutaneous injection of preparation. The death of animals was determined for a period of 24 hours after the introduction of aethaperazinum; in this case death 500/o mice began from the injection of preparation to the dose of 960 mg/kg.

Thus, LD₅₀ of aethaperazinum for mice is equal to 960 mg/kg (865-1070); LD₅₀ for rats - 405 mg/kg (367-453). During the comparison of the toxicity of aethaperazinum and aminazine it is established/installed, that the first is less toxic (Fig. 2).

Chronic toxicity was determined on rats during oral, intraperitoneal and subcutaneous introduction. The daily introduction of aethaperazinum to doses 10 and 15 mg/kg for elongation/extent of 25 days did not cause in animal toxic phenomena.

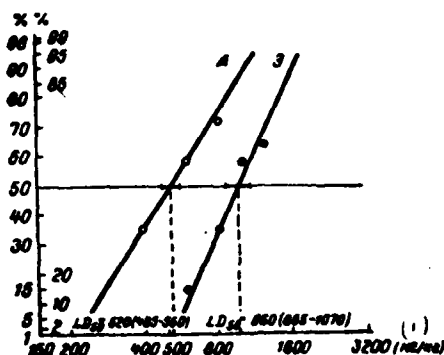


Fig. 2. Comparative evaluation of the toxic (lethal) effect/action of aethaperazinum (E) and aminazine (A) in experiment/experiences on mice. On the axis of ordinates - percentage of effect on a split scale; on the axis of abscissas - dose in the logarithmic scale; numeral in parentheses and horizontal lines designate the confidence limits of ED_{50} with $P=0.05$.

Key: (1). mg/kg.

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During the macro- and microscopic examination of the tissues of the oppressed rats of the signs of the overall toxic effect/action of aethaperazinum it is not discovered. The injection of preparation to doses 5 and 10 mg/kg during 15 days did not daily exert a substantial influence on the picture of the peripheral blood of rats.

Conclusions/derivations.

As a result of the experimental study of new neuroplegic substance - aethaperazinum - it is established/installed, that on the anti-emetic, ataractic and sedative effect/action this preparation is considerably more active than aminazine. The at the same time toxic properties of aethaperazinum are expressed to a lesser degree.

CLINICAL STUDY.

Results of study in an institute of the psychiatry of the Ministry of Public Health of the RSFSR.

The study of the clinical effect/action of aethaperazinum in clinics of the institute of psychiatry (director - Prof. D. D. Fedotov, head by clinic of late psychoses S. Yu. Zhislin, head by the separation/section of psychopharmacology - the candidate of medical sciences G. Ya. Avrutskiy, junior scientific worker O. N. Kuznetsov) the Ministry of Public Health of the RSFSR conducted during the treatment of 142 patients with the schizophrenia: 105 women and 37 men. On diagnosis the patients were distributed as follows: periodic schizophrenia was in 30, paranoid form - in 47, nuclear - in 43,

schizophrenia with the lines of various forms - in 22 patients. The duration of disease was different - from several months to 25 and more than years.

High value both for determining the onset of secondary phenomena and for the evaluation of the result of aethaperazinum therapy has the procedure of treatment used. Usually aethaperazinum appointed on 12-36 mg in a 24 hour period with a gradual (every 2-5 days) increase in the doses of preparation before the appearance of a therapeutic effect or signs of the secondary effect/action. Maximum daily doses depending on the effectiveness of treatment used 1-3 weeks and more.

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Then was conducted analogous lowering in the doses to minimum, with which did not begin the deterioration or to 12-48 mg in a 24 hour period (depending on the quality of remission, form and duration of disease). This daily dose then became supporting. The initial daily dose of preparation for patients, for the first time treated by neuroleptic substance, was 12-36 mg, for chronic patients, which well withstood previously treatment by aminazine - 24-48 mg, for resistant to treatment patients - 48-72 mg. The maximum dose of aethaperazinum for first-admission patients rarely exceeded 80-100 mg in a 24 hour period; in chronic patients it reached 200 mg, and in resistant ones

to preparation - 300 mg. The dose above 250-300 mg in a 24 hour period, as a rule, did not cause further improvement in the state of patients.

The duration of treatment in hospital was from 3 weeks to 6 months even more, but taking into account the supporting therapy it reached 2 years. The signs of therapeutic improvement in the patients whose treatment proved to be effective, were observed usually in the first 1 1/2-2 months of the use/application of aethaperazinum at sufficiently large doses. Daily dose with the supporting therapy oscillated from 12 to 60 mg. Exception were patients, resistant to the treatment; in some from them this dose reached sometimes 150 mg.

Good results are noted during treatment by aethaperazinum of the patients with periodic schizophrenia, satisfactory - with paranoid (hallucinatory-paranoid stage or variant) and the smallest effect - with nuclear forms. The analysis of clinical observations shows that the treatment with aethaperazinum causes analogous with other substances (aminazine, insulin) weather-forecast signs which do not reflect the specificity of that or other therapy, but they are the expression of the malignancy of schizophrenic process. In connection with this the comparison was conducted with the most disseminated and most studied neuroleptic substance - aminazine. All patients were subdivided into four groups.

The first group they composed 32 patients, previously treated in hospitals (from 2 to 20 times). In the given clinic these patients they treated only with aethaperazinum. This were the patients with periodic or paranoid schizophrenia, in whom were observed the aggravations against the background of supporting aminazotherapy either during change or her stopping.

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In the majority of patients the course of treatment with aethaperazinum was more shortly than during the preceding treatment in hospitals, and only in some patients approximately of the same as with therapy aminazine, in rare cases by insulin or in their combination. An improvement in the state sick more frequent was the same as during the preceding treatment, and in 5 patients with the paranoid form of schizophrenia it proved to be more significant.

In the second group there were 40 patients whose treatment by aminazine was barely effective or entirely futile. Use/application of aethaperazinum in 3 patients did not yield positive results. In 15 of patients with nuclear schizophrenia in comparison with the preceding aminazinotherapy was noted the insignificant improvement, which

nevertheless made it possible to discharge from hospital 8 people. More significant improvement (disappearance of psychotic symptomatology, incomplete criticism, unexpressed lines of schizophrenic defect) it was possible to attain in 16 patients with the unfavorably flowing periodic or paranoid schizophrenia, and also in 2 patients with the nuclear form of disease. Completely they left psychotic state 4 of patients with periodic schizophrenia.

The third group included 50 patients with the duration of disease from 5 to 25 years and the developing in recent years resistance to different forms/species of treatment (repeated aminazinothrapy, reserpine, insulin, in a number of cases electrostimulation therapy). In the majority of patients was the nuclear form of schizophrenia or the late stage of the paranoid form of this disease. In 19 patients during treatment with aethaperazinum it is not revealed of the special advantages of preparation in comparison with aminazine. At the same time in other 19 this sick group as a result of aethaperazinotherapy began certain improvement, which was being expressed in the decrease of psychotic phenomena, certain ordering of personal behavior and improvement in the relation to its native ones. In remaining 12 people after the end of treatment with aethaperazinum was observed the expressed improvement: psychotic phenomena considerably decreased, and the behavior of patients so changed to the best side which became possible to discharge them from

clinic where they were located many months, but some even are more than year.

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The fourth group consisted of 20 patients, by which aethaperazinotherapy used as the first form/species the treatments in psychiatric clinic. In 10 patients with the periodic form of schizophrenia is noted full/total/complete output/yield from psychotic state, in 8 patients, who suffered the paranoiac and paranoid syndrome of paranoid form, disappeared hallucinatory phenomena, it began deactualization of delirium and patients were discharged from hospital. Two patients with intra-hospital improvement were converted into insulinization. Approximately the same results were observed also with aminazin therapy in patients with the analogous forms of disease.

Maintenance aethaperazinum therapy more than 2 months after extraction was used in 62 patients; under dispensary conditions stopping the relapse of periodic schizophrenia or aggravation of other forms of schizophrenia was carried out in 10 patients. Aethaperazinum as preparation for the supporting and arresting therapy is not inferior on effectiveness to the aminazine; at the same time treatment by them is subjectively more easily transferred

by patients.

Aethaperazinum, as aminazine, being neuroleptic substance with wide effective range, proved to be useful and it was not inferior on effectiveness to aminazine during the treatment of the most different forms of the schizophrenia: oneroid, depressive-paranoid, paraphrenic, catatonic-paranoid, and other syndromes and their combinations with verbal hallucinosis. Certain patient in different stages began the treatments with aethaperazinum with other preparations - antidepressants, amytal with caffeine, insulin, aminazine. Aethaperazinum was more effective than aminazine in the patients, in clinical picture of whom were differently expressed phenomena of motor inhibition (from retardation to sub-stupor).

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The special features/peculiarities of therapy by aethaperazinum in comparison with aminazine they are: the smaller somniferous effect/action, the rare and weakly expressed retardation and apathy, characteristic for aminazinotherapy, the presence in series/number of the cases of the noticeably stimulating (releasing the brakes) effect/action (in patients was usually observed the less expressed retardation, than during treatment by aminazine), the action on some sides of schizophrenic defect (partial reduction of emotional

naturalness, activity of behavior, an improvement in the relation to native ones, personnel, etc.).

One of the special features/peculiarities of aethaperazinum consists in its good endurance. In contrast to aminazine during treatment with aethaperazinum in patients it was not observed the allergic reactions of skin, arterial pressure usually descended, but collaptoid state was in all in 3 patients, moreover two of them suffered cardiovascular deficiency. The tachycardia, observed frequently after the reception/procedure of preparation, was little expressed and it was not usually accompanied by the subjectively poor health; complications from the side of the blood, the liver it was not observed (in patients was controlled bilirubin of the blood); leucopenia, which appeared in one patient in whom it periodically was observed and it is earlier after the resection of uterus and X-ray therapy, it disappeared before stopping of aethaperazinum therapy. In 2 patients during treatment by preparation appeared the pains in gastrocnemius muscles, while in 3 sharpened chronic exchange arthritis (two of them treatment by aethaperazinum they interrupted).

About good endurance of preparation tells also the fact that for treatment by aethaperazinum were converted several patients, who badly/poorly transferred other neuroleptic substances; 4 patients in view of onset in them during treatment by aminazine and

trifluoperazine of the convulsive phenomena; 2 - as a result of an increase of the bilirubin in the blood with aminazinotherapy; 1 - in connection with edema of face after the use/application of aminazine, and then dichlorpromazine; 3 - due to the development of aminazine dermatitis; 1 - as a result of the aggravation of bronchial asthma. In these all patients the treatment with aethaperazinum complications did not cause.

Most frequent secondary phenomena were the extrapyramidal disturbances/breakdowns: acatnsia - for 48 patients, tremor - in 18, constraint - in 18. All these phenomena, as a rule, easily were arrested by the reception/procedure of antiparkinsonian preparations (best anything artane) and rarely required lowering the doses. In 7 patients with organic deficiency rarely were observed the spasms of look, while in 2 - beginning of treatment with aethaperazinum obtained correctives, extrapyramidal disturbances/breakdowns did not arise. Several patients sometimes complained about deterioration in the view (disturbance/breakdown of convergence).

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To the majority of patients appointed the bitartrate of aethaperazinum and only 1/4 - dihydrochloride. Some patients during the specific period they treated by the foreign preparation Trilafon.

The given factual data tell about the great variety of clinical observations. It is necessary to note that the collaptoid states in patients were observed only during treatment of them with Trilafon or by dihydrochloride of aethaperazinum; use/application latter/last more frequently caused in patients weakness, somnolency, apathy, vertigo, dryness in mouth, etc.

Results of study at the Institute of psychiatry of the Academy of Medical Sciences of the USSR.

In the institute of psychiatry of AMN of the USSR (director - Prof. A. V. Snezhnevskiy, senior scientific workers A. B. Smulevich and V. Ye. Galenko, junior scientific worker V. Kuznetsov) the clinical study of aethaperazinum conducted in essence during the treatment of the patients with schizophrenia with paranoid, hallucinatory-paranoid, depressive-paranoid and catatonic states. Additional testing preparation was carried out in several patients with the diagnosis of involutional depression, manic-depressive psychosis, traumatic psychosis and Huntington's chorea.

Of 60 patients with schizophrenia there were 10 men and 50 women. Primarily they entered into the hospital of the institute of

23 patients, and is repeated - 37 patients, it is earlier long (not less than the year) treated by aminazine and other methods of therapy, but it is unsuccessful. Aethaperazinum appointed inside usually on 3 or 6 mg of 2-3 times in day. Subsequently of every 2-7 days the daily dose of preparation they increased to 9-12 mg and finished to 30-40 mg during the day; they continued to increase the dose through 2-3 weeks.

During the treatment of first-admission patients the dose of aethaperazinum was usually from 24 to 72 mg in a 24 hour period, for patients with the tightening forms of disease even than earlier treated by other substances - from 72 to 100 mg in a 24 hour period; maximum dose reached in some patients to 324 mg.

Especially good tolerance in the relation to aethaperazinum was noted in patients, than earlier treated by aminazine.

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Treatment with aethaperazinum in the group of first-admission patients was continued 1-3 months, patients with the tightening forms of disease - from 3 to 6 months. However, the majority of patients after the end of the course of treatment obtained the supporting therapy with aethaperazinum at dose from 24 to 48 mg in a 24 hour

period. By patient with uninterrupted course diseases the supporting therapy conducted from 3 to 4 months, but after its stopping again appeared morbid symptoms.

Many patients were treated with aethaperazinum in combination with other medicinal/medicamentous substances: somniferous ones of barbituric series/number, antidepressants (tophranyl, niamide), aminazine, insulin, Bekhterev's mixture, antiparkinsonian preparations, pouring in of glucose with vitamins, injections of strychnine. This complex treatment did not create complications.

Analysis of clinical data showed that the effect/action of aethaperazinum barely differs from the effect/action of aminazine. During treatment by aethaperazinum is noted favorable effect on the state of a hallucinatory-delirious excitation, the softening of delirious intensity/strength and anxieties, weakening of the intensity of hallucinatory manifestations, but in the cases of significant improvement the complete disappearance of hallucinatory-delirious symptoms. The especially good effect/action of preparation was observed in the patients with schizophrenia with the prolonged periodic course of the diseases, in which noticeably weakened hallucinatory, delirious and catatonic symptoms, which indicates the advantage of aethaperazinum in comparison with aminazine.

As a result of treatment by aethaperazinum in patients was noted the ordering of behavior, stopping failure of food, appeared criticism in the relation to the previous delirious statements; patients became neater, independently *etc* and serviced/maintained themselves; in some the state so was improved that they were discharged for conducting the supporting therapy. In patients with the agitated depression (involuntional psychosis, schizophrenia) began rapid damping, was improved sleep and appetite. The reverse development of the symptoms of depression occurred considerably slower, in connection with which by certain patient they appointed additionally tophranyl.

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Positive results were observed also with the therapy of patients with the maniacal states (manic-depressive psychosis, schizophrenia), appearing in essence in people of elderly age, suffering atherosklerosis.

In patients with the limply elapsing form of schizophrenia and the depersonalization syndrome or with the phenomena of asthenic depression, in spite of lasting (to 3 months) therapy with

aethaperazinum by sufficiently high doses (150 mg in a 24 hour period), and also the use/application of other neuroleptic substances, improvement is not noted.

During treatment with aethaperazinum in patients appeared the following secondary phenomena. During the first days of the reception/procedure of preparation appeared the symptoms of parkinsonism of different degree; in comparison with the effect/action of aminazine in sick more frequently appeared extrapyramidal hyperkineses, dystonias; the earliest and predominant symptom were motor restlessness/anxiety, "restlessness" (actasia); then was observed the constraint of motions, mimicry, tremor of extremities, the general/common/total retardation; in certain cases these phenomena were matched with sadness, depressive statements. All these secondary symptoms were arrested well by the reception/procedure of Deparkin, Dinezin, Ritalin. But if the preparations indicated did not damp extrapyramidal phenomena, then it was necessary to decrease the doses of aethaperazinum.

As far as system is concerned vegetative, then in many patients after the first receptions/procedures of aethaperazinum incidentally, and during prolonged use/application at large doses stably descended the arterial pressure; it appeared the dryness of the mucous membranes of the cavity of mouth, somnolency, apathy, pallor of face,

weakness, in some patients - tachycardia, in rare cases - a collaptoid state.

As mental symptom in several patients appeared phenothiazine depression, insomnia.

The analyses of the blood, urine and these investigations of the function of the liver did not show substantial changes.

Subsequently preparation they appointed by 36 additional patient, who mainly suffered schizophrenia. Treatment was conducted through the same scheme, moreover were confirmed the obtained previously results. In 4 sick from this group aethaperazinum was applied in connection with the intolerance of other neuroleptic substances which was developed in the onset of hepatitis. Aethaperazinum did not cause complications.

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Results of study at the department of midwifery and gynecology of the I Moscow Order of Lenin medical institute im. I. M. Sechenov.

Climacteric syndrome is the complication of the age rearrangement of hypothalamic nerve centers and is characterized by

the increased excitability and their reactivity, and therefore the use/application of sedative substances with this syndrome it is most substantiated and pathogenetically directed.

The typical clinical manifestations of climacteric syndrome include: the inflows/bosses of fever to head and the upper surfaces of body, which are accompanied by sweating, chill, weakness, first pain and vertigo, excessive irritability, excitability, tearfulness, touchiness, disturbance/breakdown of sleep, view, efficiencies, lowering in the memory, etc. With climacteric syndrome they secrete three basic clinical variants: typical, complicated and atypical with the preponderance of primary diencephalic disturbances/breakdowns.

The clinical tests of aetnaperazinum in the department of midwifery and gynecology (head - doctor of the medical sciences Ye. M. Vikhlyayev, doctor T. M. Dondukov) of the therapeutic (evening) faculty of I MOLMI were carried out during the treatment of 70 dispensary patients, at age from 40 to 60 years, predominantly with the complicated forms of climacteric syndrome. Patients were found under observation from 5 months to 1 year.

Treatment with aetnaperazinum was conducted through the manufactured scheme with the individual selection of doses. They appointed preparation in tablets on night, beginning with the dose of

2-4 mg, not more than 12 mg in a 24 hour period. Then dose they increased to the onset of therapeutic effect, and then again lowered.

The expressed therapeutic effect was noted in patients, who obtained in a 24 hour period from 2 to 12 mg of preparation. To course the treatments by duration from 6 to 16 weeks appointed from 200 to 1300 mg of preparation.

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In the majority of patients as a result of treatment with aethaperazinum sufficiently rapidly was reached the good effect, which was expressed in the disappearance of the basic psychotic and vasomotor manifestations: ceased inflows/bosses, sweating, headaches, vertigo; gradually was normalized sleep, disappeared a feeling of fear, depression, tearfulness, touchiness, was restored efficiency, appeared cheerfulness, etc. The effectiveness of treatment and the designation/purpose of the course dose of preparation to a considerable extent depend on the severity of climacteric syndrome and associated diseases.

Improvement in state was observed already toward the end of the 1st week of treatment, completely symptoms disappeared in 1-2 months. In some patients during treatment with aethaperazinum were noted the

secondary phenomena: tachycardia, tremor, constraint, restlessness/anxiety, insomnia, weakness. They were revealed/detected with the designation/purpose of the optimal doses of preparation and usually they disappeared after their decrease. From the side of liver and bile-secretion ducts complications were not observed.

Results of study in the department of midwifery and gynecology of the II Moscow medical institute im. N. I. Pirogov.

In the obstetrical clinic of II MMI (leader - Prof. A. A. Lebedev, staff physician N. V. Gordeycheva) aethaperazinum was used during treatment 48 women with the first or repeated pregnancy, suffering vomiting in different stages of disease. Patients were at age from 18 to 42 years, the period of pregnancy was from 6 to 12 weeks. Patients were divided into two groups.

In the first group, which consists of 30 pregnant females with the phenomena of neurosis, that suffer vomiting, was conducted the treatment with aethaperazinum. In the second group, where entered 18 become pregnant with toxicosis and dystrophia, in view of the build-up/growth of changes in metabolism was used the combined therapy (vitamins C, E, groups B, introduction of fluids/liquids and of salt solutions, oxygenotherapy, physiotherapy) with the simultaneous introduction of aethaperazinum.

Preparation appointed orally in tablets on 0.012 g of 2-3 times in the day through 30 minutes after reception/procedure foods. The course of treatment was continued 10-14 days.

During treatment with aethaperazinum in the patients of the first group was observed a more rapid, than with aminazinothrapy, improvement in the general state and stopping vomiting, which contributed to more rapid discharge from the hospital.

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Most distinctly came to light the advantages of the combined therapy with the use/application of aethaperazinum in the second group in such phases of vomiting in pregnant females as toxicosis and dystrophia: whereas improvement began during the first days of treatment, while the combined therapy without aethaperazinum gave effect only through 1-2 weeks.

In the first group the vomiting in patients ceased approximately/exemplarily through 2 weeks, but the secondly - on 7-10 days it is later.

As a result of aethaperazinum therapy the vomiting greatly rapidly was decreased, and then ceased, which made it possible to regulate the nourishment of pregnant females, facilitated the introduction to a duodenal-feeding fluid/liquid, it contributed in combination with other medicinal preparations of the standardization of the function of central nervous system, it helped an improvement in the disrupted metabolism, is exerted the favorable influence on psychics/psyche. The decrease of vomiting from the first days of treatment by preparation improves the mood of pregnant females, moves the faith/belief in the success of the conducted treatment, what is critical moment/torque in the course of disease.

After treatment with aethaperazinum in 47 pregnant females began the recovery. In one woman with the combined mitral flaw of heart without the disturbance/breakdown of blood circulation the combined therapy did not give effect and pregnancy was interrupted from medical readings. The relapse of disease is noted in 4 pregnant females, but after treatment under dispensary conditions in them began recovery.

Results of study at the Central dermatovenerologic institute.

The clinical tests of aethaperazinum were carried out in the section of dermatology and the separation/section of children's

dermatology of TSKVI (substitute/deputy of director on scientific part - Prof. A. A. Studnitsin, Prof. N. S. Smelov, Prof. M. A. Rozentul).

In the section of dermatology under observation were found 17 patients, of them 12 men and 5 women. At age from 19 to 30 years there were 6 patients, from 30 to 40 years - 3, from 40 to 50 years - 3, from 50 to 60 years - 4, 64 years - 1 patient.

Diffusion neurodermatitis was observed in 4 patients, chronic eczema in the stage of aggravation - in 6, seborrheal eczema - in 4, mushroom-shaped mycosis - in 2, the innate/inherent Broca's ichthyosiform erythroderma - in 1 patients.

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The duration of disease comprised prior to 1 years in 4 patients, from 1 year to 2 years - in 2, from 2 to 5 years - in 4, from 5 to 10 years - in 2, and in 5 sick disease it was continued from 17 to 24 years. Diffusion rashes on skin are noted in 15 patients, the smaller spread of rashes (in 4-5 sections) - in two.

The sharply pronounced buzzing/itch was observed in 2 patients, expressed - in 10, moderate - in 5. The disturbance/breakdown of

sleep is noted in 14 patients: poor sleep - in 9, agitated - in 5. In spite of the disseminated rashes, in 3 sick sleep was good.

Aethaperazinum by patient appointed at the following individual doses: on 1 tablet during day was obtained by 1 patient, on 1-2 tablets - 10, from 1 to 3 tablets - 3, from 1 to 4 tablets - 3 patients. Treatment by preparation lasted from 4 to 9 days in 5 patients, moreover in four aethaperazinum abolished in connection with the onset of secondary phenomena, aggravation diseases or unsatisfactory result of the treatment; from 15 to 25 days it was treated by 9, also, from 28 to 40 days - 3 patients. Clinical recovery not in one of the patients it is noted; significant improvement began in 5, improvement - in 2, aggravation - in 2, did not have effect 3, treatment is ended in 5 (2 of these patients also did not have effect).

By all patient in connection with the significant spread of rashes and the sharply pronounced inflammatory phenomena, infiltration in stricken areas they prescribed the external, most frequently damping skin symptomatic treatment (Unna's cream, 20/o salicylic ointment, sulicianolin, 20o/o zinc butter, washes, etc.). By certain patient were used also therapeutic pastes.

During the evaluation of the effect of aethaperazinum on the

character/nature of sleep and the intensity of buzzing/itch is established/installed a significant improvement in the sleep in 3 patients, improvement - in 4; sleep did not change in 10 (in 2 patients was observed somnolency by day). The disappearance of buzzing/itch was noted in 2 patients (in the odnogo on the 8th day, in another on the 14th day of treatment), the significant decrease of buzzing/itch - in 7, the decrease of buzzing/itch - in 3; in 2 patients after short-time improvement the buzzing/itch was renewed with previous force. An increase in the buzzing/itch was observed in 1 patients, his intensity did not change in 5 people. This served as basis for stopping of further therapy with aethaperazinum.

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In 3 patients, who obtained in a 24 hour period from 0.036 to 0.048 g of aethaperazinum, are noted the secondary phenomena: permanent headaches, the intensity/strength of gastrocnemius muscles, the perception of severity in head, the tremor of hands.

Positive clinical results during treatment with aethaperazinum of basic disease, and also an improvement in the sleep were established/installed in 7 of the 17 patients, and only in 9 of the 17 was lowered the intensity of buzzing/itch.

In the separation/section of children's dermatology aethaperazinum was prescribed for 43 children, suffering that being pruritic of the dermatoses when conventional antipruritic means (Dimedrol [Diphenhydramine], diazoline, pipolphen, etc.) did not give effect. At age from 1 year to 5 years there were 14 children, from 5 to 12 years - 12 and from 12 to 16 years - 17.

To children from 1 year to 5 years preparation they appointed at the doses of 3-6 mg, and from 5 to 12 years - on 6-12 mg to the reception/procedure of 2 times in day. To children older than 12 years in the absence of effect dose raised to 12 mg.

The effectiveness of preparation was expressed in the significant decrease of buzzing/itch, an improvement in the sleep, the reverse development of skin process. Children's majority transferred preparation completely satisfactorily, without secondary phenomena. In 5 children were observed the headaches, vertigo, overall weakness, while in 3 children, furthermore, the spasms of muscles and in one child - epileptiform phenomena.

Conclusions/derivations.

Aethaperazinum is strong neuroleptic substance with wide effective range. It possesses significant therapeutic activity and at

the same time is of low toxicity.

In its effect/action the preparation is very close to aminazine. Under the effect of aethaperazinum in patients with the various forms of schizophrenia was noted the softening, and in some the disappearance of a hallucinatory-delirious symptomatology.

In patients with the periodic or paroxysmal course of schizophrenia and from different by degree resistance to aminazine the translation/conversion into treatment with aethaperazinum causes an improvement in the state, which facilitates care of them or is shortened the period of the stay in hospital.

Aethaperazinum is transferred well by patients and is not inferior on effectiveness to aminazine.

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This makes it possible to use extensively aethaperazinum under the dispensary conditions, and to also prescribe it for those patients, which badly/poorly transfer aminazinothrapy. However, in comparison with aminazine aethaperazinum more frequently are caused in patients the secondary phenomena in the form of extrapyramidal hyperkinesis, which rapidly disappear with prescription of correctives. The

advantage of aethaperazinum in comparison with other preparations of phenothiazine series/number consists in the fact that the sedative and anti-psychotic effect is reached more rapidly, also, with the aid of considerably smaller doses (from 48 to 72 mg), than during treatment by aminazine.

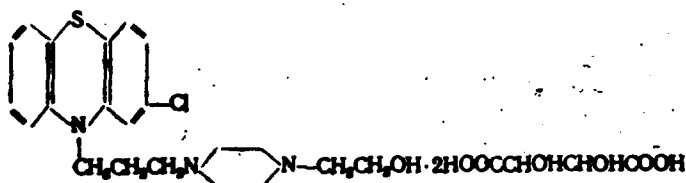
The high effectiveness of aethaperazinum is noted during the treatment of patients with the diverse variants of climacteric syndrome, including in combination with hypertonic disease/sickness/illness/malady, and also with the therapy of the vomiting of pregnant females. With the heavily elapsing forms of disease the use/application of a preparation in combination with other medicinal agents leads to a rapid improvement in the state and stopping of vomiting. The correctly carried out treatment prevents the onset of relapse.

With a strict observance of age dosages aethaperazinum is a good antipruritic substance in the patients with pruritic dermatosis when other sedative and ganglion-blocking preparations do not give sufficient result. Aethaperazinum is recommended to combine with different antihistaminic preparations (Diazoline, Dimedrol, pipolphen, etc.)

INSTRUCTION ON THE USE OF AETHAPERAZINUM

Is affirmed by the pharmacological committee of Ministry of Public Health of the USSR on 16 November, 1963.

Aethaperazinum is dihydrochloride of
2-chloro- γ -[4-(β -hydroxyethyl)-piperazinyl-1]-propyl)-phenothiazine:



and on chemical structure it corresponds to the foreign preparations: chloropiperazine, perphenazine, Trilafon.

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This is the white fine-crystalline powder, water-soluble and physiological solution. With standing in the light/world aethaperazinum and its solutions are decomposed/expanded. The solutions of aethaperazinum withstand/maintain sterilization by boiling.

Aethaperazinum - neuroplegic and anti-emetic substance, which possesses the wide spectrum of pharmacological activity, similar mainly to the spectrum of the effect/action of aminazine. On the

series/number of the forms/species of the central effect (anti-emetic, tranquilizing and sedative) aethaperazinum is more active than aminazine. The adrenolytic effect/action of preparation is expressed to a lesser degree than in the aminazine; in comparison with the latter the preparation is less toxic.

Indications of use.

Aethaperazinum is recommended for use/application in therapeutic practice during the same readings, as the aminazine: 1) in psychiatric practice for the treatment of the states of maniacal excitation with circular psychosis, schizophrenia and other mental diseases; a depressive-agitated state in patients with presenile psychosis; acute/sharp catatonic excitation, hallucinatory-delirious and stuporous states; hypochondriac syndrome with the obtrusive ideas; firm insomnia in the patients with the neuropsychic diseases and so forth; 2) in obstetrical practice during the treatment of pregnant females with the indomitable vomiting; 3) in dermatological - as sedative substance for removing/taking the skin buzzing/itch; 4) in therapy and surgery - as sedative and anti-emetic substance.

Method of use/application and dose.

In the psychiatric practice aethaperazinum is prescribed in

tablets on 4 and 8 mg after food. The first time the dose of aethaperazinum must not exceed 12 mg during day. Subsequently the dose of preparation is established/installed individually depending on the state of the patient; the daily doses of preparation can be increased to 60 mg in a 24 hour period. By the chronic and resistant to aminazine patient aethaperazinum it is possible to appoint at large doses - to 150 mg in a 24 hour period. Maximum one-time dose must not exceed 100 mg, diurnal - 200 mg.

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During the use/application of aethaperazinum in combination with somniferous substances it is necessary to consider its capacity to deepen and to lengthen the effect/action of somniferous substances; therefore patients must be found under the observation of medical personnel. Initially after the reception/procedure of preparation patients must lie/rest not less than 1 1/2-2 hours in connection with the possibility of the onset of orthostatic collapse. The duration of treatment with aethaperazinum is from 10 to 60 days and depends on the mental and somatic state of patients.

In the obstetrical, therapeutic and surgical practice aethaperazinum as anti-emetic substance is prescribed in tablets on 4-8 mg of 3-4 times in day.

Possible complications and fight with them.

The use/application of large doses of aethaperazinum can be accompanied by the development of orthostatic collapse and extrapyramidal disorders. The abolition of preparation or lowering the dose leads to the disappearance of these phenomena. Extrapyramidal disturbances/breakdowns it is possible to arrest by the introduction of cholinolytic substances (Cyclodol) and Diprazin.

Contraindications.

The use/application of aethaperazinum is contraindicated during the damage of the function of the liver (cirrhosis, Botkin's disease), of kidneys and hemopoietic organs/organs, poisoning by narcotics, analgetics or somniferous substances, with endocarditides.

Form of issue.

Aethaperazinum is produced in the tablets with coating, which contain on 0.004 g (4 mg) and 0.01 g (10 mg) of substance.

Storage conditions.

Store aethaperazinum with precaution, in the hermetically sealed bottles of dark glass, in dry fresh place. The period of aptitude is shown on label.

Approximate sample/specimen of formula.

Rp. Aethaperazini 0.004.

D. t. d. N. 30 in tabul.

S. on 1 tablet 3-4 times a day.

DISTRIBUTION LIST

DISTRIBUTION DIRECT TO RECIPIENT

<u>ORGANIZATION</u>	<u>MICROFICHE</u>	<u>ORGANIZATION</u>	<u>MICROFICHE</u>
A205 DMATC	1	E053 AF/INAKA	1
A210 DMAAC	2	E017 AF/RDXTR-W	1
B344 DIA/RDS-3C	9	E403 AFSC/INA	1
C043 USAMIIA	1	E404 AEDC	1
C509 BALLISTIC RES LABS	1	E408 AFWL	1
C510 AIR MOBILITY R&D	1	E410 ADTC	1
LAB/FIO			
C513 PICATINNY ARSENAL	1	FTD	
C535 AVIATION SYS COMD	1	CCN	1
C591 FSTC	5	ASD/FTD/NIIS	3
C619 MIA REDSTONE	1	NIA/PHS	1
D008 NISC	1	NIIS	2
H300 USAICE (USAREUR)	1		
P005 DOE	1		
P050 CIA/CRB/ADD/SD	2		
NAVORDSTA (50L)	1		
NASA/NST-44	1		
AFIT/LD	1		
LLL/Code L-389	1		
NSA/1213/TDL	2		